Economic Burden of *Salmonella* Infections in the United States

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Abstract

The aim of this study is to evaluate medical expenditures and lost productivity associated with burden of *Salmonella* infections. We used laboratory confirmed number of *Salmonella* cases and corresponding multipliers to estimate the burden of illness using the method adopted by Foodborne Diseases Active Surveillance Network (FoodNet) at Centers for Disease Control and Prevention (CDC). The medical costs estimates are retrospective analysis of reimbursement records from MarketScan data. We identified patients with a diagnosis of salmonellosis using ICD-9 CM codes from the MarketScan 1993–2001 databases. Productivity loss from the nonfatal cases of *Salmonella* was calculated using the distributions of lost workdays and household services due to the illness. Statistical value of life approach was used to estimate the costs due to premature deaths. We also compared the costs for the gastrointestinal salmonellosis to the cost for the invasive salmonellosis. Confidence intervals around the cost estimates were calculated using a Monte Carlo simulation technique. Estimated average economic burden due to *Salmonella* was $210 per outpatient, $5,797 per inpatient with gastrointestinal infection, $16,441 per inpatient with invasive infection and $4.63 million per premature death. Total economic burden due to *Salmonella* in the United States was estimated at $2.8 billion (95% CI: $1.6 to $5.3 billion) annually, which is approximately $2,472 per case of *Salmonella* infection. The cost estimate is largely driven by the number of premature deaths followed by average cost of hospitalization. Defining the risk factors for fatal outcomes may help target treatment and preventive strategies.

Keywords: *Salmonella*, gastrointestinal, invasive, productivity loss, medical costs, FoodNet, MarketScan

Introduction

Although U.S. food supply has high level of safety, illnesses from foodborne pathogens cause billions of dollar loss to the society in terms of medical costs and productivity loss. It has been estimated that foodborne illnesses caused by known and unknown pathogens result approximately 76 million illnesses, 325,000 hospitalizations, and 5,000 deaths in the United States every year (Mead, 1999). Among several foodborne illnesses, salmonellosis is a major illness caused by consumption of *Salmonella* contaminated foods. The infection sometimes spreads from the intestines to the blood stream, and then to other body parts. The disease causes significant burden of illness in the form of morbidity and mortality. Infected person may need to seek medical care and visit physicians. In severe cases patients are hospitalized and some patients may die prematurely due to complications. Generally the elderly, the infants and the immune compromised individuals are affected severely by the *Salmonella* (Frenzen, et al., 1999). An estimated 1.4 million cases of salmonellosis occur every year in the United States. Salmonellosis imposes a large economic burden on individual and the society. It has also been estimated that approximately 16,000 salmonellosis patients are hospitalized and 600 persons die each year due to *Salmonella* infection related diseases (Mead, 1999). Human salmonellosis associated costs include costs incurred by the person becoming ill or by the parties on behalf of the ill person. Direct costs are measured in dollar amount, which include medical costs and lost productivity. Cohen et al. 1978 assessed the patient related economic costs in an outbreak of salmonellosis in 1976. According to the study,

total cost to an individual was related to the severity of illness and extent of medical care. Direct medical costs and lost productivity were accounted in the study. In an average cost incurred by an individual was $645 of which 68 percent was in medical cost, 26 percent in productivity loss and 6 percent in miscellaneous costs. In 1985, indirect cost of single episode of non-complicated gastroenteritis was estimated at $215 if the ill person did not visit physicians and the cost was $348 if visited physicians (Garthright, et al., 1988). Roberts, 1987 updated medical costs and productivity loss using various price indices from Bureau of Labor Statistics and also estimated the average value of lost life using Landefeld and Seskin (1982) method (Roberts, 1988). Landfield and Seskin method includes financial losses due to death but excludes costs associated with leisure time and pain and suffering. Frenzen et al, 1999 estimated the economic burden of *Salmonella* infections in the United States and the annual cost estimates ranged from $0.5 to $2.3 billion depending on the method used (human capital approach and labor market approach) to assign value to the human lives (Frenzen, et al., 1999). Center for Food Safety and Applied Nutrition (CFSAN) used labor market approach to estimate the economic value of lost lives. CFSAN used about $5 million per lost life to assess the economic burden of diseases. In addition to medical costs and productivity loss, CFSAN also took account of losses due to pain and suffering in cost estimates (Raybourne et al.). The economic impacts of salmonellosis from different studies are hard to compare since estimates are from different time periods, geographic regions and methods. Furthermore, in most of the studies, there exist great deal of uncertainty surrounding the estimates of total number of illnesses, proportions of cases by the severity groups of the disease and the average costs of medical care and productivity loss. In general, medical care data are

not normally distributed but are skewed strongly to the right, which make the cost estimates biased and inefficient. Providing the costs estimates along with the underlying probability distributions give better picture of economic burden of illness.

Methods:

The economic burden estimated in this study includes medical costs, lost productivity incurred by the *Salmonella* infected individuals, and value of lost lives resulting from premature deaths. Data were obtained from various sources as listed in table 1. These data provide information on the distributions of disease incidence and costs of medical care. Total number of cases is estimated from using laboratory conformed cases and multipliers obtained from disease surveillance system.

Table 1: The data and their sources

Data	Sources
Distributions of Salmonella cases: Self-care, Outpatients, Inpatients and Deaths	1.FoodNet publication (Voetsch et al., 2004)* 2.Foodborne Diseases Survillance Network 3.Public Health Laboratory Information System
Medical Costs: Outpatients costs, Inpatient costs, Prescription drugs costs	MarketScan Databases from 1993 to 2001 (Inpatient Admission, Outpatient Claims and Prescription Drugs)**
Lost Productivity: Work days lost, wages, employments	1. MarketScan Databases from 1993 to 2001 2. Economic Research Service (ERS) 3. Bureau of labor statistics
Value of life	Economic Research Service, USDA

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**MarketScan database contains medical care claims reimbursement records for the medical services and prescription drugs. Prescription drugs data were not available from 1993 to 1996 MarketScan database.

Total number of *Salmonella* cases may vary by year. There are several factors that determine the number of cases and existing practices of collecting data have high potentials for introducing errors. In order to deal with uncertainty on estimates it would be more useful to give the distributions of burden estimates.

Table 2: Reported laboratory confirmed cases and multipliers to estimate the total burden of Salmonella

Multipliers	Distributions of multipliers					
	Bloody diarrhea (30% to 70% of total)			Non-bloody diarrhea (30% to 70% of total)		
	Min	Mean	Max	Min	Mean	Max
Labs identify *Salmonella*	1.1	1.4	1.43	1.1	1.4	1.43
Physicians obtain specimens	1.0	1.0	1.43	3.33	5.5	10
Patients seek medical care	3.33	6.8	10.0	6.66	8.6	20

Adapted from Voetsch et al, 2004, "FoodNet Estimate of the Burden of Illness Caused by Nontyphoidal *Salmonella* Infections in the United States".

Cost of medical care is another important information required to estimate the economic impact of a disease. In this study, costs of medical services and prescription drugs data were extracted from the MarketScan database. MarketScan database contains retrospective medical care claim data maintained by the MedStat Group at Ann Arbor, Michigan. We used 1993 to 2001 MarketScan database. Data consisting of inpatient admissions (1993 to 2001), outpatient claims (1993-2001) and prescription drug claims (1997 to 2001) from MarketScan database were utilized to estimate the costs. All the claim records marked identified *Salmonella* as one of the diagnosis codes were isolated from the database using ICD-9 CM codes. In these extracted medical records, *Salmonella* infections were listed either as primary diagnosis or as the secondary diagnosis. Illnesses were categorized into two groups depending on the type of the diagnosis code of infections: gastrointestinal infections (ICD 9 CM Codes: 003.0) and invasive infections (ICD 9 CM Codes: 003.1, 003.21, 003.22, 003.23, 003.24, 003.29). The grouping is done to analyze the variation in treatment costs for invasive *Salmonella* and the gastrointestinal *Salmonella.* Outpatient costs and inpatient cost for invasive and

gastrointestinal illnesses are different, therefore, we analyzed costs by the types of *Salmonella* infections. The cost due to productivity loss was calculated on the basis of workdays and household services lost due to illnesses. National employment rates, wage distribution and statistical value of lost lives were taken into consideration while estimating the productivity loss.

Burden of illness:

CDC reports laboratory confirmed total numbers of salmonellosis cases annually (Appendix A) using data reported through disease outbreaks, passive surveillance systems: national notifiable diseases surveillance system and public health laboratory information system, and active surveillance system: foodborne diseases active surveillance system. Medical care multiplier, physician multiplier, laboratory multiplier and proportion of bloody and non-bloody diarrhea were used to estimate the total number of salmonellosis cases in US based on the laboratory confirmed salmonella cases reported to the CDC. A recent publication by Voetsch et al 2004: "FoodNet estimate of the burden of illness caused by nontyphoidal *Salmonella* infections in the United States" in the journal of Clinical Infectious Disease, discusses the method used and results on burden estimates.

The burden of salmonellosis causes significant morbidity and mortality in the United States. Severity of the disease is an important aspect of burden of illness. Persons with mild salmonellosis did not seek physician or emergency department care for their illness. Persons with moderate illness visited at least one physician but were not hospitalized. Persons with severe illness were hospitalized at least once during this period. Centers for Disease Control and Prevention regularly conduct active surveillance for several

foodborne diseases including salmonellosis. Using the surveillance data and U.S. census data, CDC makes the national estimates of total cases of salmonellosis along with proportion of disease outcomes. In the surveillance system, most culture confirmed cases of *Salmonella* infection are reported to health official. However, there exist strong possibility of under reporting. Persons infected with *Salmonella* may not develop symptoms that require medical attention. Sometime physician may not collect specimen for laboratory tests. Similarly the entire specimen forwarded for laboratory testing may not be tested or may not be identified correctly. It has been estimated that 30,000 to 40,000 cultures confirmed cases of non-typhoidal *Salmonella* represent only one percent to five percent of the actual number of *Salmonella* cases in the U.S. population (Chalker, 1988). Different multipliers to estimate the total number of *Salmonella* cases as described in appendix A are listed in table 1. Applying these multipliers it has been estimated that average annual number of *Salmonella* cases in U.S. population are 38.6 times of the culture confirmed cases (Voetsch, 2004).

Economic burden of salmonellosis:

Cost of illness is an estimate of direct medical costs associated with treatment of salmonellosis and the indirect cost of lost time or wages that may be incurred by either a patient or by an unpaid caregiver. Cost elements include physician visits, hospitalization, and prescription drugs. We recognize that the costs of pain and suffering might be substantial. The monetary value of pain and suffering are difficult to estimate with accuracy (United States Environmental Protection Agency, 2003) and the direct medical costs of treating diseases provides a lower-bound estimate of the cost of illness. Costs per patient represent average expenditure incurred by a patient for one episode of

salmonellosis. Multiple years cost data from medical care database were adjusted for inflation by using medical component of consumer price index. We categorized salmonellosis cases as mild, moderate, and severe by type of medical care sought during the illness. Costs of hospitalization are generally higher if the salmonella infections are invasive (blood stream infection) compared to the gastrointestinal infections (non blood stream infection). We analyzed the costs of hospitalization for invasive infections and gastrointestinal infections separately.

Medical costs:

We categorized illness from mild to severe depending on the type of medical care sought by the patients. Medical costs for persons treated as outpatients include fees paid for ambulance, emergency room services, physician charges and laboratory tests. Inpatient costs include fees paid to hospital, physician, and the prescription drugs expenditures incurred for the patients who were hospitalized.

Productivity loss:

Productivity loss is the income forgone because of illness. The human-capital approach was used to estimate the productivity loss for the nonfatal cases of salmonellosis. Various factors such as employment rates, wages, and numbers of workdays lost were used to estimate the lost productivity. Non-wage activities: house keeping, childcare, and other activities were also taken into account. Data on length of hospitalization were obtained from the MarketScan database (1993 to 2001 inpatient admissions tables). Since there were no reliable data on the lost workdays for outpatients and inpatients after hospital discharge, we adopted the assumptions made by ERS in similar studies. According to the Occupational Employment Statistics Survey data from the Bureau of Labor Statistics,

median wages of US workers were $136.10 per day in the year 2001. In addition to lost wages, ill person is not able to perform household services. Average value of household services in US was estimated as much as $10,805 per person annually (Haddix, et. al, 2000). Adjusting for inflation, average value of household services becomes $30.45 per day per patient.

Value of lost lives:

Economic burden that *Salmonella* places to the society also comes from disease mortality. Although it is small, there is a risk of dieing from salmonellosis related complications. It is hard to place a dollar value on the lost human lives. Willingness to pay for mortality risk reductions (statistical value of life) is one of the standard approaches to estimate the value of lost lives. Suppose a new hypothetical food safety intervention reduces the annual risk of dying of a *Salmonella* infection by 0.0001. In a community of 10,000 people the intervention is expected to result in 1 fewer death from *Salmonella* infection each year. Using this reasoning, if each person in that population of 10,000 is willing to pay $20 a year for reducing the risk, the statistical value of a life is present value of stream of cash flow of $20,000 per year for the reminder of the life. Value of lost lives depends on the age distribution of patients who died of salmonellosis related complications. Discount rates used to estimate the present value of future incomes also influence the value of life.

Results and discussion:

Patients with milder illnesses do not visit physicians and they may purchase over the counter medications and do not go to the work for certain period of time. There are no

relevant data to estimate the direct medical costs for the mild cases of salmonellosis therefore we estimated only the lost productivity for this severity group. Average productivity loss for was $53 under the assumptions that the persons with mild illness lose only about 0.5 day of work and household services.

Outpatient costs: Average medical costs for patients of gastrointestinal and invasive *Salmonella* infections are given in table 3 to compare the average per patient (outpatient) costs. Difference in average outpatient costs for invasive and gastrointestinal infection is not statistically significant. Outpatient costs due to the *Salmonella* infection may reach as high as $16,000.

Table 3: Outpatient costs by types of infections (MarketScan 1993-2001)

Salmonella type	N	Mean	Std. Dev	25 percentile	Median	75 Percentile
Invasive	392	294.55	697.54	56.68	106.26	229.38
Gastrointestinal	2,596	299.04	742.58	54.12	98.25	221.27
All Cases	2,988	298.46	736.69	54.45	99.29	222.68

N=Number of unique cases of S*almonella* recorded in MarketScan data

The range of cost is wide and most of the observations are clustered to the lower end of the distribution. The overall mean cost of medications per episode of illness was $298. Median cost ($99) was substantially lower than the mean costs, suggesting that distribution of outpatient costs was skewed toward right. Fewer salmonella cases were driving the mean cost higher. Patients with invasive S*almonella* and gastrointestinal *Salmonella* had the mean costs: $295 and $299 respectively. Statistical analysis indicated that the differences in costs of medications between the types of infection were not significant (Table 4). We assumed that outpatients are not able to perform their

regular duty during illness for about 1.6 days in average. Value of lost wages and household services were estimated as $169 per outpatient.

Inpatient costs: Overall mean direct medical cost of hospitalization per case of salmonellosis was $7,734. Median cost ($4,789) was substantially lower than the mean costs. Hospitalized patients who were diagnosed with invasive S*almonella* and gastrointestinal *Salmonella* had the mean costs of $16,215 and $5,981 respectively (table 4).

Table 4: Average inpatient costs by type of infections (MarketScan 1993-2001)

Salmonella type	N	Mean	Std. Dev	25 percentile	Median	75 Percentile
Invasive	136	16,215	23,222	5,576	9,466	16,200
Gastrointestinal	657	5,981	8,222	2,820	4,385	6,381
All Cases	793	7,734	12,760	2,990	4,789	7,502

N=Number of unique cases of S*almonella* recorded in MarketScan data

Statistical analysis indicated that the difference in costs of hospitalization between the types of infection was significant. Inpatients cost per episode of S*almonella* related hospitalization ranges from $240-149,087. The range is wide and most of the observations are concentrated to the lower range in the distribution. Standard deviations are high. Few influential data points made the range wider and larger standard deviation. Average costs difference by type of infection are statistically significant at 0.01 probability level. In general, mean or the median medical costs are higher for the invasive infection, compared with gastrointestinal infections. According to the MarketScan data average lengths of hospitalizations were 8.9 days and 4.2 days for invasive and gastrointestinal infections respectively. We assumed that patients are not

able to resume their regular duty immediately after the hospital discharge and stay in rest for about 1.6 days in average. After taking account of distribution of US wages, employment rates, five working days per week and lost household services, average productivity losses among hospitalized patients were $1,110 and $604 per episode of invasive and gastrointestinal infections respectively.

Costs of fatal cases: Value of lost lives was treated as an annuity. In 1990, USDA Economic Research Service assumed the present value of the annuity at the age of 36.5 years as much as $5,000,000, as estimated by Kip Viscusi from labor market data. After adjusting for inflation, the value of life becomes $6,618,087 in 2001 dollars. Under the assumptions of constant annual value of life, 3% discount rate, underlying age distribution of *Salmonella* related deaths (multiple causes of death certificates) and life expectancy; average estimated value of lost lives was $4,624,171 in 2001dollar value.

Monte Carlo Simulation:

Most of the estimates on variables used in the cost analysis have uncertainty. Expected or the average values do not show the impact of uncertainty. Therefore, the point estimates may not give the decision-maker a complete picture of possible burden of illness and its economic consequences. A Probability distribution of relative occurrence for each possible outcome gives the better information than the traditional descriptive analysis. Ranges of burden of illness and associated costs directly related to the level of underlying uncertainly in the variables involved in the estimates. Distributions of health care costs associated with *Salmonella* infections are not normal and skewed with large positive tail. Analyzing the costs entering the distributions of variables show all the possible outcomes with relative frequencies/probabilities.

Estimation of location and variation parameters of distribution is an important task in data analysis. The simulation results are given in appendix B and appendix C. Most of the fitted distributions of disease outcomes have zero skewness indicating that simulated data are normal. Distributions of medical care costs have positive coefficients, which imply that distributions have long tails to the right. Positive skewness of health care cost is a normal phenomenon. Inpatient and outpatient costs summarized in Appendix B (simulated cost data) are somewhat different than the cost extracted from MarketScan database listed in table 3. Total economic burden due to *Salmonella* are calculated by the Monte Carlo Simulation method instead of simply multiplying the total number of cases by the average costs. Estimated annual economic burden (medical costs and productivity loss) of salmonellosis is about $2.8 billion (95 % CI: $1.6 to $5.3 billion). Fig. 2 and fig. 3 show the relative frequency of distributions of economic burden. Distribution of costs is dramatically affected by the method used to value the lost human lives. If the lives were valued by the human capital approach then the estimated mean economic burden would be about $453 million.

Conclusion:

Salmonellosis is a major foodborne illness caused by consumption of *Salmonella* contaminated foods. Epidemiological estimates of burden of *Salmonella* infection have been revisited. Medical costs and productivity loss by the severity of illness have also been estimated to translate the burden of illness into the economic burden by calculating societal costs which include direct healthcare expenditures and productivity losses. The medical costs estimates are retrospective analysis of reimbursement records from MarketScan data. Confidence intervals around the cost estimates were calculated using a

Monte Carlo simulation to deal with the uncertainty in the cost estimates. Estimated average medical expenditure and productivity loss due to *Salmonella* was $210 per outpatient, $5,797 per inpatient with gastrointestinal infection, $16,441 per inpatient with invasive infection. Total economic burden due to *Salmonella* in the United States was estimated at $2.8 billion (95% CI: $1.6 to $5.3 billion) annually. However, if lost lives were valued by the human capital approach the average costs would be dramatically lower. Total cost estimate is driven by premature deaths followed by cost of hospitalization.

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Appendix A: Distribution of *Salmonella* related illness and disease outcomes (1990-2001)

Year	Lab-Confirmed Reported Cases	Estimated cases of *Salmonella*					
		Total cases	Self care	Outpatients	Inpatients (Invasive)	Inpatients (Gastro)	Premature Deaths
1991	40,443	1,436,618	1,271,099	144,333	3,530	17,051	606
1992	34,688	1,232,188	1,090,222	123,794	3,027	14,625	519
1993	36,917	1,311,367	1,160,279	131,749	3,222	15,565	553
1994	37,522	1,332,858	1,179,293	133,908	3,275	15,820	562
1995	41,222	1,464,289	1,295,582	147,113	3,598	17,380	617
1996	39,035	1,386,603	1,226,846	139,308	3,407	16,458	584
1997	34,608	1,229,347	1,087,708	123,509	3,020	14,591	518
1998	33,971	1,206,719	1,067,688	121,236	2,965	14,323	509
1999	32,782	1,164,483	1,030,318	116,992	2,861	13,821	491
2000	33,310	1,183,239	1,046,913	118,877	2,907	14,044	499
2001	31,675	1,125,161	995,526	113,042	2,764	13,355	474
Average	36,016	1,289,567	1,140,990	129,559	3,168	15,306	544

*Estimated based on the laboratory confirmed cases, laboratory multipliers, Physician multipliers, medical care multipliers.
**Adopted from Mead et al. (1997).

Appendix B-1 Monte Carlo Simulation: detail statistics of key variables

Statistics	Total Burden (Per year)	Expected burden ($ Per case)	Total Salmonella (Cases per year)	Outpatient Cost $	Inpatient cost $ (Invasive)	Inpatient cost $ (GI)*
Minimum	2,300,435,000	1,789	567,738	0	486	415
Maximum	6,241,845,000	5,788	4,237,218	21,377	511,898	146,971
Mean	2,788,166,000	2,472	1,395,387	211	16,441	5,796
Std Deviation	304,935,200	361	460,865	715	27,232	6,370
Skewness	1	1	1	17	8	9
Kurtosis	13	7	6	434	116	150
Mode	2,605,684,000	2,307	1,253,904	27	5,060	3,468
5 Percentile	2,380,997,000	1,930	833,274	13	2,341	1,539
10 Percentile	2,421,065,000	2,004	907,987	20	3,146	1,954
25 Percentile	2,526,077,000	2,215	1,061,917	38	5,111	2,889
50 Percentile	2,779,571,000	2,439	1,305,938	79	9,264	4,336
75 Percentile	3,013,454,000	2,721	1,625,152	174	17,502	6,716
80 Percentile	3,041,384,000	2,792	1,718,037	214	20,644	7,462
90 Percentile	3,123,256,000	2,965	1,989,777	390	33,388	10,229
95 Percentile	3,210,036,000	3,056	2,245,501	679	51,776	13,924

*GI=Gastrointestinal *Salmonella* infection

Appendix B-2 Monte Carlo Simulation: detail statistics of key variables

Statistics	Self care (Cases/year)	Outpatients (Cases/year)	Invasive Inpatients	Non-invasive Inpatients	No. of Deaths	LOS Days (Invasive)*	LOS Days (Non-invasive)
Minimum	995,526	113,042	2,764	13,355	474	0	0
Maximum	1,295,582	147,113	3,598	17,380	617	109	33
Mean	1,138,840	129,646	3,171	15,297	543	9	4
Std Deviation	113,448	12,975	316	1,517	54	10	3
Skewness	0	0	0	0	0	3	3
Kurtosis	1	1	1	1	1	19	18
Mode	995,526	113,042	2,764	13,355	474	2	2
5 Percentile	995,852	113,078	2,765	13,359	474	1	1
10 Percentile	997,476	113,267	2,770	13,387	475	2	2
25 Percentile	1,019,070	115,913	2,837	13,715	486	3	2
50 Percentile	1,130,490	129,172	3,153	15,215	539	6	3
75 Percentile	1,259,128	143,456	3,505	16,904	600	11	5
80 Percentile	1,274,848	145,070	3,546	17,099	607	13	6
90 Percentile	1,292,032	146,783	3,589	17,333	615	20	7
95 Percentile	1,295,019	147,061	3,596	17,372	617	27	10

*LOS=Length of hospital stay in days

Appendix C: Figures

Fig. 1: Distribution total annual cases of *Salmonella* in U.S.

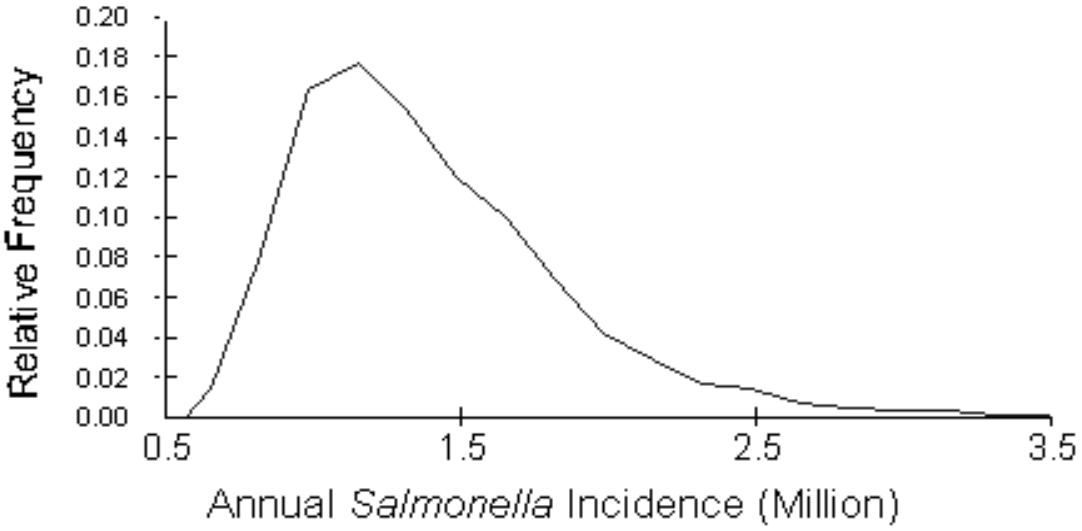

Fig 2: Economic burden due to *Salmonella* in U.S. (human capital approach)

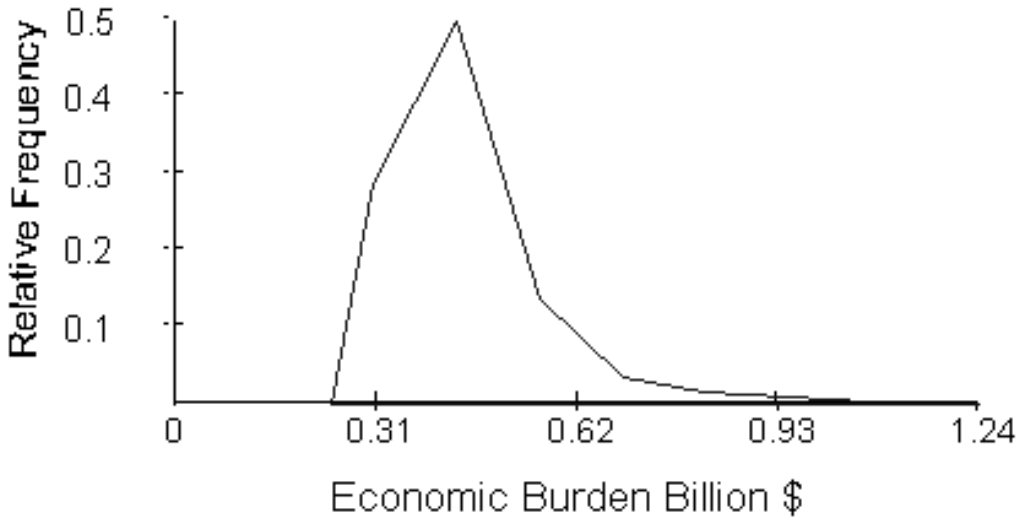

Fig 3: Economic burden due to *Salmonella* in U.S. (labor market approach)